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Applicants' Specification at Page 7, lines 15-17. New Claims 47-50 have been added to cover preferred embodiments of the invention. Support for new Claim 47 can be found in Applicants' specification at Page 5, line 33 to Page 6, lines 1-2. Support for new claims 48-50 can be found in Applicants' Specification at Page 50, line 30 bridging Page 51, line 26, Page 60, lines 3-15, Page 61, lines 5-23 and Page 62, lines 5-11.

Upon entry of the amendments presented, Claims 1-50 remain in the application. An additional claims fee is due as a result of these amendments. This additional claims fee is charged to the Assignee's Deposit Account via the attached cover sheet.

### **Invention Synopsis**

The present invention, as now claimed, relates to topical compositions for the treatment of microbial infections on the skin or scalp which include a polyvalent metal salt of pyrithione and include a metal ion source wherein the pH of the composition is greater than 7 when the metal ion source is a zinc salt. The present invention also relates to methods of treating microbial infections of the skin or scalp using such compositions. The present invention further relates to methods of regulating or stimulating hair growth or inhibiting or reducing hair loss using such compositions.

### **Response to Restriction Requirement**

Restriction of Applicants' claimed invention has been required under 35 U.S.C. §121. The Office Action contends that restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-25, 28-30, 36-38 and 42-46, drawn to topical composition, classified in class 424, subclass 435.
- II. Claims 26-27, drawn to an anti-dandruff composition, classified in class 514, subclass 852
- III. Claim 31, drawn to a method of treating athlete's foot, classified in class 514, subclass 858
- IV. Claim 32, drawn to a method of treating microbial infections, classified in class 514, subclass 858.

- V. Claim 34, drawn to a method of treating fungal infections, classified in class 424, subclass 404.
- VI. Claim 35, drawn to a method of treating dandruff, classified in class 514, subclass 132.
- VII. Claim 33, drawn to a method of improving appearance, classified in class 424, subclass 132.
- VIII. Claim 39, drawn to a method of regulating hair growth, classified in class 514, subclass 852.
- IX. Claim 40, drawn to a method of stimulating hair growth, classified in class 514, subclass 852.
- X. Claim 41, drawn to a method of inhibiting or reducing hair loss, classified in class 514, subclass 852.

Election of a single disclosed species was further requested for each of the following:

1. Election of a metal ion source for Claims 1, 6, 7, 8, 9, 27, 28 and 36
2. Election of a pyrithione for Claims 2 and 3
3. Election of a surfactant for Claim 17
4. Election of an anti-microbial active agent for Claim 23
5. Election of a conditioning agent for Claim 25

For the purpose of complying with the election request, Applicants provisionally elect, with traverse, Group I, Claims 1-25, 28-30, 36-38, and 42-46, drawn to a topical composition, classified in class 424, subclass 435, holding Claims 26-27, 31, 32, 33, 34, 35, 39, 40 and 41 in abeyance under the provisions of 37 C.F.R. § 1.142(b) until final disposition of the elected claims.

For the purpose of complying with the election request, Applicants provisionally elect with traverse the following species: 1) zinc salts for Claims 1, 6, 7, 8, 9, 27, 28 and 36; 2) zinc pyrithione for Claims 2 and 3; 3) anionic surfactants for Claim 17; 4) ketoconazole for Claim 23; and cationic polymers for Claim 25.

The restriction requirements are respectfully traversed herein.

The Examiner submits that the Inventions III, IV, V, VI, VII, VIII, IX and X are unrelated, stating that inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects. The Examiner has asserted that in the instant case, the different inventions can be used for a variety of methods. The Examiner further submits that Inventions I and II are related as combination and subcombination and asserts that in the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because it can be used as an anti-fungal composition, wherein the subcombination has a separate utility as an anti-dandruff composition. Lastly, the Examiner submits that Claims 1, 6, 7, 8, 9, 27, 28 and 36, Claims 2 and 3, Claim 17, Claim 23; and Claim 25 are generic to a plurality of disclosed patentably distinct species and requires election of a single disclosed species for prosecution on the merits.

Applicant respectfully submits that the compositions of Group I and Group II are so closely interrelated and in order to preserve unity of invention, both groups should be prosecuted in the same application. The PTO examination would be simplified and duplicate searching eliminated by pursuing one as opposes to two or more applicants.

Applicants respectfully submit that it would not be unduly burdensome to search for and examine all of the claims in the present application. Restriction is proper only when the inventions are independent or distinct as claimed and it would be unduly burdensome to search for and examine all of the inventions in a single application (see MPEP 803). It is submitted that prosecution of all of the claims in this present single application would also be permitted and would indeed be quite appropriate. It is submitted that in the present case, any prior art search set up for the compositional claims of Group I and Group II would be coextensive with that for the method claims of Groups III to Group X, because the novel compositions and methods involve the same compositional material.

### Art Rejections

#### 35 U.S.C. § 103(a)

Claims 1-25, 28-30, 36-38 and 42-46 are rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Wiese (U.S. 5,227,156). Applicants respectfully traverse this rejection.

Wiese discloses that the activity of a thiazolinone preservative, in an anti-dandruff shampoo containing pyrithione, is maintained by adding a stabilizer comprising a zinc compound. Specifically, Wiese discloses an aqueous anti-dandruff shampoo comprising up to about 40% of a surfactant, from about 0.1% to about 2% zinc pyrithione, from about 1 to about 30 ppm of a preservative selected from the group consisting of 5-chloro-2-alkyl-4-isothiazolin-3-one, 2-alkyl-4-isothiazolin-3-one, wherein the alkyl is selected from the group consisting of methyl, ethyl, butyl, propyl and mixtures thereof, from about 0.001% to about 1% of a preservative stabilizer comprising a zinc compound selected from the group consisting of a zinc salt of an organic acid, a zinc salt of an inorganic acid, zinc oxide, zinc hydroxide, and mixtures thereof, and the balance comprising water.

However, the present invention, as now claimed, is neither disclosed nor made obvious by Wiese. The present invention is directed toward a topical composition for treating microbes, in order to inhibit or prevent the growth on the skin or scalp of said microbes, comprising from about 0.001% to about 10%, by weight of the composition, of an anti-microbial active selected from the group consisting of polyvalent metal salts of pyrithione, from about 0.001% to about 10%, by weight of the composition, of a metal ion source selected from group consisting of zinc salts, copper salts, silver salts, nickel salts, cadmium salts, mercury salts, bismuth salts, and mixtures thereof; and a topical carrier for the anti-microbial active and the metal salt; wherein the weight ratio of the metal source to the anti-microbial active is from about 5:100 to about 5:1 and wherein at least 50% of the anti-microbial active is insoluble in the composition and further wherein the pH of the composition is greater than 7 when the metal ion source is a zinc salt. Wiese, on the contrary, teaches a shampoo composition which has a neutral to slightly acidic pH (Column 3, lines 64-66). Surprisingly, the Applicants of present invention have found that the pH of the composition at a neutral to slightly acidic pH does not provide the benefit of increasing the antidandruff efficacy by the use of a metal ion source, specifically a zinc salt, in combination with polyvalent metal salts of pyrithione. As now amended, the present invention states that the pH of the composition is greater than 7 when the metal ion source is a zinc salt.

Further, Wiese's examples teach away from the present invention. Wiese exemplifies very low levels of zinc oxide and zinc chloride in Example 1 and Example 2.

Example 1 teaches 0.05 % by weight zinc chloride and Example 2 teaches 0.07% by weight of zinc oxide and 0.05% by weight of zinc chloride. In the present invention, Examples 6, 7, 12, 15, 16, 19 and 20 disclose aqueous compositions comprising zinc sulfate present at 2% and 1%, respectively. Clearly one of skill in the art would not be lead to the present invention by the teachings of Wiese. If one of skill in the art were to make the exemplified compositions of Wiese, they would not arrive at the present invention's compositions comprising a zinc salt.

Wiese is directed toward a completely different invention. In Wiese, the use of a zinc compound is solely for the purpose of stabilizing a thiazolinone specific preservative. There is no disclosure or suggestion in Wiese of the combination of a metal ion source with an polyvalent metal salt of pyrithione wherein it has been surprisingly found that the antidandruff efficacy can be dramatically increased by the use a metal ion source such as copper, silver, nickel, zinc, cadmium, mercury and bismuth salts in combination with polyvalent metal salts of pyrithione. Further, it would not be obvious to one of skill in the art to look to Wiese in an attempt to improve efficacy for anti-dandruff and skin care as taught by the present invention. Wiese is simply disclosing a method to stabilize a thiazolinone specific preservative. Wiese specifically states in Column 1, lines 26-30 that surprisingly it has been found that the activity of a thiazolinone preservative in a zinc pyrithione shampoo can be maintained by adding a stabilizer comprising a zinc compound. One of skill in the art would be not be lead by Wiese, which is "maintaining" the activity of a thiazolinone preservative, and arrive at a method to significantly improve the efficacy for anti-dandruff and skin care as taught by the Applicants' invention.

#### **No Prima Facie Case**

Applicants respectfully traverse the obvious rejection, as Wiese does not establish a prima facie case of obviousness because Wiese does not teach or suggest all of the Applicants' claim limitations. Wiese does not teach a topical composition comprising a metal ion source in combination with an anti-microbial active selected from the group consisting of polyvalent metal salts of pyrithione [wherein the composition has a pH of greater than 7 when the metal ion source is a zinc salt] Contrary to the present invention's claim limitations, Wiese teaches aqueous shampoo compositions wherein the pH is

neutral to slightly acidic. Wiese does not disclose the present invention's claimed element wherein the composition has a pH greater than 7. Therefore, there is no prima face case of obviousness since Wiese does not teach or suggest all of the Applicants' claim limitations.

In light of the arguments presented herein, it is respectfully submitted that the rejection of the claims under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a) be withdrawn.

### Conclusion

Applicants have made an earnest effort to place their application in proper form and distinguish their claimed invention from the prior art which was applied in the September 10, 2001 Office Action. WHEREFORE, consideration of this application, consideration of the accompanying claims and claim amendments submitted herewith, withdrawal of the rejections under 35 U.S.C § 102 and 35 U.S.C § 103, and allowance of Claims 1-50 are respectfully requested.

Respectfully submitted,  
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March 11, 2002  
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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Claims:**

Claim 1 has been amended as follows:

1. (AMENDED) A topical composition for treating microbes, in order to inhibit or prevent the growth on the skin or scalp of said microbes, comprising:

a) from about 0.001% to about 10%, by weight of the composition, of an anti-microbial active selected from the group consisting of polyvalent metal salts of pyrithione;

b) from about 0.001% to about 10%, by weight of the composition, of a metal ion source selected from group consisting of zinc salts, copper salts, silver salts, nickel salts, cadmium salts, mercury salts, bismuth salts, and mixtures thereof; and

c) a topical carrier for the anti-microbial active and the metal salt;

wherein the weight ratio of the metal source to the anti-microbial active is from about 5:100 to about 5:1 and wherein at least 50% of the anti-microbial active is insoluble in the composition and further wherein the pH of the composition is greater than 7 when the metal ion source is a zinc salt.